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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/058,825	01/30/2002	Roderick John Scott	0623.1160001/LBB/GLL	2437

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EXAMINER
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BAUM, STUART F

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 10/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/058,825

**Applicant(s)**

SCOTT, RODERICK JOHN

**Examiner**

Stuart F. Baum

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 July 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 20,21,62-67,69,71,76-78 and 80-93 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 20,21,62-67,69,71,76-78 and 80-93 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>7/27/2006</u> . | 6) <input type="checkbox"/> Other: _____  |

**DETAILED ACTION**

1. The amendment and Jacobsen Declaration filed 7/27/2006 have been entered.
2. Claims 20-21, 62-67, 69, 71, 76-78, and 80-93 are pending and are examined in the present office action.

Claims 1-19, 22-61, 68, 70, 72-75 and 79 have been canceled.

3. Rejections and objections not set forth below are withdrawn.
4. The text of those sections of Title 35, U.S. Code not included in this office action can be found in a prior office action.

***Information Disclosure Statement***

5. The Office action received in U.S. Application 10/966,482 was considered but is not appropriate for printing on the cover of a U.S. patent.

***Indefiniteness***

6. Claims 20-21, 62-67, 69, 71, 76-78, and 80-93 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection includes dependent claims.

Claim 20 is indefinite in the recitation "a sequence whose transcription product comprises a partial or full length Arabidopsis DNA methyltransferase 1 (Met1) sequence." Applicants have disclosed "Therefore, the designation Arabidopsis Met1 sequence will always refer to the sequence of Accession No. L10692..." (page 13 of Remarks filed 11/7/2005, 1<sup>st</sup> full paragraph).

Said sequence is a DNA sequence, therefore, it is unclear how a transcription product can be a DNA sequence and not a mRNA sequence.

Claim 62 is indefinite in the recitation “a sequence whose transcription product comprises a partial or full length Zea mays sequence orthologous to the Arabidopsis methyltransferase 1 (Met1) sequence.” Applicants have disclosed “Therefore, the designation Arabidopsis Met1 sequence will always refer to the sequence of Accession No. L10692...” (page 13 of Remarks filed 11/7/2005, 1<sup>st</sup> full paragraph). Said sequence is a DNA sequence, therefore, it is unclear how a transcription product can be a DNA sequence and not a mRNA sequence.

These rejections are maintained for the reasons of record set forth in the Official action mailed 1/27/2006. Applicant’s arguments filed 7/27/2006 have been fully considered but they are not persuasive.

Applicants contend that it is known in the art that a transcription product is RNA and that the transcription product is a faithful copy of the DNA template from which the transcription product was transcribed (page 8 of Remarks, 2<sup>nd</sup> paragraph).

The Office contends that it is known in the art that the transcription of DNA creates a RNA molecule. But, the Office contends that Applicant’s claim is unclear because Applicant states that the transcription product is a partial or full length Arabidopsis DNA methyltransferase 1 (Met1) sequence, and it is stated that said Met1 will *always* refer to the sequence of Accession No. L10692 (as stated above). Therefore, given Applicant’s explicit definition, the Office maintains that the claims as written, are unclear for the reasons given in the office action mailed 1/27/2006.

***Written Description***

7. Claims 20-21, 62-67, 69, 71, 76-78, 80-93 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These rejections are maintained for the reasons of record set forth in the Official action mailed 1/27/2006. Applicant's arguments filed 7/27/2006 have been fully considered but they are not persuasive.

Applicants contend "the written description requirement does not require the applicant to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed" (page 9 of Remarks, 1<sup>st</sup> full paragraph). Applicants contend that "the Federal Circuit has held that "(1) examples are not necessary to support the adequacy of a written description (2) the written description standard may be met [] even where actual reduction to practice of an invention is absent; and (3) there is not per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." Falkner v. Inglis, 448 F.3d 1357, 79 U.S.P.Q.2d 1001 (Fed. Cir. 2006) (page 9 of Remarks, bottom paragraph). Applicants contend "with respect to point (3) that "where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here "essential genes"), satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences"" (paragraph bridging pages 9 and 10 of Remarks). Applicant contends that according to the Federal Circuit decisions in Capon and Falkner, a per se requirement that partial

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Arabidopsis Met1 or Zea mays orthologous sequences not be recited in the specification (page 10 of Remarks, 1<sup>st</sup> full paragraph).

The Office contends that the fact pattern of the instant application is not the same as the fact pattern associated with the Capon and Falkner cases. In the Capon case the claims were drawn to chimeric proteins, wherein the pieces which made up the chimeric proteins were known in the art. In the Falkner case, the claimed sequences were known in the art. In the instant application, the Office contends the genus of Met1 sequences is not known in the art. Applicant discloses that the Arabidopsis Met1 sequence was cloned by Finnegan et al (1993; listed in IDS) and that Finnegan et al disclose the Met1 sequence as Accession Number L10692 (page 12 of Remarks filed 11/7/2005, 7<sup>th</sup> paragraph). Applicants further state “Therefore, the designation Arabidopsis Met1 sequence will always refer to the sequence of Accession No. L10692...” (page 13 of Remarks filed 11/7/2005, 1<sup>st</sup> full paragraph). The Office contends that the Zea mays Met1 sequence is disclosed in NCBI accession number AF06343. Applicants have not disclosed a representative number of sequences from a representative number of plants, encoding an Arabidopsis Met1 homologous protein. It is not clear from the listed accession numbers if the disclosed sequences are the orthologues of the Arabidopsis Met1 sequence. In addition, Applicants have not disclosed essential elements of the genus of partial or full length Arabidopsis Met1 sequences. In addition, Applicants have not disclosed a single partial sequence that can be used to down-regulate one or more methylating enzymes present in a plant and produce plants whose seeds have a modified endosperm.

Applicant contends that the complete carrot, corn, pea and tomato Met1 sequences were known of the earliest priority date and Applicant references NCBI Accession numbers

AF007807, AF063403, AF034419, and AJ002140 (page 10 of Remarks, 1<sup>st</sup> full paragraph).

Applicant contends one of ordinary skill in the art would have been aware that Met1 nucleotide sequences have a high degree of sequence identity and that there are regions that are highly conserved. Applicant points to Finnegan et al pages 227-229 (*Ibid*). Applicant contends that there exist regions of 75%, 76%, 82% and 91% sequence identity between sequences encoding an Arabidopsis and Zea mays DNA methyltransferase (*Ibid*).

The Office acknowledges that other methyltransferases were known prior to the filing date of the instant application, but not all methyltransferases can be used in applicant's invention of a method for the production of modified endosperm. Even Finnegan et al states "The identification of multiple DNA methyltransferases in plants raises the question of whether the proteins recognize and methylate cytosines in different sequence contexts, whether the different enzymes catalyze maintenance or de novo methylation, or whether they are active in different tissues or stages of development. There is evidence supporting the notion that plant methyltransferases may differ in target specificity" (page 229, bottom paragraph). The Office contends Applicant has not disclosed a representative number of partial Met1 sequences, or even full length sequences that can be used to down regulate one or more DNA methylating enzymes and produce a plant whose seeds have a modified endosperm. Therefore, the Office contends Applicant is not in possession of the broadly claimed genus.

Applicant contends that the specification teaches techniques to down-regulate MET1 (paragraph bridging pages 10 and 11). Applicant contends and the Jacobsen Declaration contends that one of ordinary skill in the art would understand that a partial sequence would comprise more than two nucleotides, and Applicant contends that the Examiner's interpretation

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of “partial” does not correspond to the interpretation that would have been given by one of ordinary skill (paragraph bridging pages 11 and 12 of Remarks and paragraph 11 of Jacobsen Declaration).

The Office contends that given the lack of an explicit definition of “partial” the Office contends Applicant’s claims are drawn to nucleic acid sequences comprising any di-nucleotide of the Arabidopsis Met1 sequence.

Lastly, Applicant contends Examples 3 and 4 disclose a construct having an Arabidopsis MET1 antisense sequence targeted to the female germ line and which is less than full-length (page 12 of Remarks, top paragraph).

The Office contends that Example 3 discloses prophetically making antisense fragments. The Office contends that the specification does not disclose any partial sequences that can be used to down-regulate one or more DNA methylating enzymes and produce a plant whose seeds have a modified endosperm.

### ***Scope of Enablement***

8. Claims 20-21, 62-67, 69, 71, 76-78, 80-93 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for increasing the amount of endosperm in an Arabidopsis or Brassica seed or increasing the weight of an Arabidopsis or Brassica seed comprising a construct comprising a full length MET1 DNA sequence operably linked to the AGL5 promoter, wherein the sequence is in antisense orientation, or wherein the MET1 DNA sequence is isolated by RT-PCR from Arabidopsis using the primers MET1F of SEQ ID NO:5 and MET1R of SEQ ID NO:6 and Arabidopsis and



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Brassica plant transformation therewith, does not reasonably provide enablement for claims broadly drawn to a method of modifying the endosperm from any plant comprising down-regulating any DNA methylating enzyme using a sequence whose transcription product comprises a partial or full length Arabidopsis Met1 sequence or which comprises a partial or full-length Zea mays sequence orthologous to the Arabidopsis Met1 sequence, or wherein the nucleic acid is a partial or full length sequence in sense or antisense orientation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. These rejections are maintained for the reasons of record set forth in the Official action mailed 1/27/2006. Applicant's arguments filed 7/27/2006 have been fully considered but they are not persuasive.

Applicant contends, as stated in the Jacobsen Declaration, paragraph 14, that a showing of hypomethylation caused by transforming plants with the Arabidopsis Met1 sequence in antisense orientation has no bearing on whether one of ordinary skill would have expected a decrease in the degree of overall DNA methylation (page 13 of Remarks, 2<sup>nd</sup> paragraph). Applicant contends the Examiner failed to identify a single instance where downregulation of a Met1 gene failed to reduce the degree of methylation (page 13 of Remarks, 3<sup>rd</sup> paragraph).

The Office contends that the claims are not just drawn to decreasing the degree of overall DNA methylation, but rather the claims are drawn to decreasing DNA methylation for the production of modified endosperm.

Applicant and the Jacobsen Declaration consider the Examiner's interpretation of claims 20 and 62, in regards to the interpretation of "a construct comprising a promoter *and* another

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sequence” to be unreasonable. Applicant contends one of ordinary skill would have interpreted these claims to mean that a promoter that targets expression to a female germ line and not to mean that the promoter is in a position not necessarily next to the sequence of interest (page 13 of Remarks, 4<sup>th</sup> paragraph and paragraph bridging pages 13 and 14).

The Office contends that Applicant’s claims do not specify that the promoter and sequence of interest be operably linked. The claims only specify that the nucleic acid molecule comprise a promoter *and* a sequence of interest. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant contends the Examiner’s interpretation of “partial” as meaning any two nucleotides is not in line with an understanding by one skilled in the art (page 14 of Remarks, 2<sup>nd</sup> paragraph). Applicant contends that one of ordinary skill in the art would know that partial sequences, including 3’ and 5’ regions, can work to down-regulate a gene, and Applicant has listed U.S. patents and non-patent literature (paragraph bridging pages 14 and 15). Applicant contends that the Arabidopsis and Zea mays Met1 sequences were known at the time of filing and it would have been routine for one of ordinary skill to screen for partial sequences that would work to down-regulate the endogenous Met1 gene (page 15 of Remarks, 2<sup>nd</sup> full paragraph).

The Office contends that given the lack of an explicit definition of “partial” the Office contends Applicant’s claims are drawn to nucleic acid sequences comprising any di-nucleotide of the Arabidopsis Met1 sequence. The Office acknowledges that there are reports of 3’ and 5’ regions that work to down-regulate a gene but not all 3’ or 5’ regions will work. It is known in

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the art that the only way to determine which 3' or 5' regions will work to down-regulate an endogenous gene is to test it empirically. In the instant application, Applicant has not provided any guidance for determining which partial sequence of the Arabidopsis Met1 or which partial sequence of the Z. may orthologue of the Arabidopsis Met1 will work to down-regulate one or more DNA methylating enzymes and produce a plant whose seeds comprise a modified endosperm. Applicant has not provided guidance for which partial sequence of the Arabidopsis Met1 can be used to down-regulate methyltransferases in monocots or which partial sequences from Zea mays Met1 can be used in dicots to down-regulate methyltransferases and produce plants whose seeds have a modified endosperm. Given the lack of disclosure and the unpredictability in the art as stated in the office action mailed 1/27/2006, undue trial and error experimentation would be required by one of skill in the art to practice the claimed invention.

Applicant contends that the Fourgoux-Nicol et al, Gutteron and Emery et al references, which were cited by the Examiner demonstrating unpredictability, in fact demonstrate that the claimed invention is enabled (page 16 of Remarks, 1<sup>st</sup> and 2<sup>nd</sup> paragraphs). Applicant and the Jacobsen Declaration contend that the data from the Fourgoux-Nicol et al reference can be extrapolated to mean that the Arabidopsis and Zea mays Met1 sequences would hybridize with each other (page 16 of Remarks, 3<sup>rd</sup> paragraph).

The Office contends that the Fourgoux-Nicol et al reference was cited in regards to using degenerate primers. It is no longer applicable. The Office maintains the Gutteron and Emery et al references demonstrate unpredictability.

Applicant and the Jacobsen Declaration contend that one of ordinary skill would have expected that in general heterologous partial or full length sequences can be used to down-

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regulate endogenous genes based on the teachings of Elkind et al., Hibino et al., Bolitho et al. and Salehuzzaman et al (page 17 of Remarks, top paragraph). Applicants disclose additional references which utilize antisense technologies (page 17 of Remarks, 1<sup>st</sup> full paragraph to page 18, 5<sup>th</sup> paragraph). Applicant and the Jacobsen Declaration state “While the Gutterson reference reports that a chrysanthemum chalcone synthase sense sequence did not suppress a petunia chalcone synthase, such a result does not mean that sequences with imperfect homology would necessarily be ineffective for down-regulation (page 18 of Remarks, bottom paragraph).

The Office contends that there are references disclosing the use of antisense technology or sense technology. The Office does not dispute the fact that antisense technology can be used to down-regulate an endogenous gene. The enablement rejection is directed toward the full breadth of the claims. The Office contends that the enablement rejection does not go against the use of antisense technology, but rather, the enablement rejection is directed toward Applicant’s claims drawn to a method for the production of modified endosperm comprising introducing into any plant a partial or full-length Arabidopsis or Zea mays Met1 sequence in antisense orientation, wherein transcription of said sequence is effective for down-regulating one or more DNA methylating enzymes present in a plant. Applicant has only disclosed down-regulating the Met1 gene in Arabidopsis or Brassica creates seeds with a modified endosperm, wherein Applicant uses a nucleic acid sequence encoding the Arabidopsis Met1 gene. Applicant has not disclosed any partial sequence of the Arabidopsis Met1 gene or any partial sequence of the Zea mays orthologue of the Arabidopsis Met1 gene, that can be used to down-regulate the full length endogenous gene in any plant, monocot or dicot, and produce seeds with a modified endosperm. Applicant has not shown that down-regulating any methyltransferase produces seeds with a

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modified endosperm. Applicant has not disclosed that a promoter not operably linked to the sequence of interest will direct the expression of said sequence. The Office contends plants possess a multitude of methyltransferases. Applicant has not disclosed which regions of the Met1 gene can be used for down-regulating the endogenous gene that will not down-regulate the other multitude of methyltransferases present in a plant. Given the lack of disclosure as discussed above, given the unpredictability in the art as discussed in the previous office action mailed 1/27/2006, given the state-of-the-art and the breadth of the claims, undue trial and error experimentation would be required by one of skill in the art to practice the broadly claimed invention.

9. No claims are allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

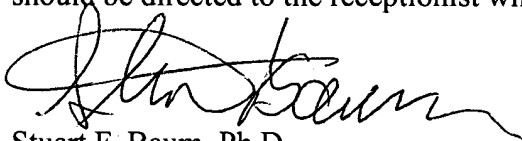
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached at 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

A handwritten signature in black ink, appearing to read 'Stuart F. Baum', with a stylized, flowing script.

Stuart F. Baum Ph.D.

Primary Examiner

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October 13, 2006